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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/749,601	12/28/2000	Nicholas C. Nicolaides	01107.00069	4817

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EXAMINER

KRUSE, DAVID H

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 10/01/2002

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicant No.

09/749,601

Applicant(s)

NICOLAIDES ET AL.

Examiner

David H Kruse

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 June 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-125 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-125 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. § 121:
 - I. Claims 1-3, 13, 18, 19, 25, 27, 34, 40, 42, 47, 48, 52, 77, 83 and 84, drawn to a method of making a hypermutable cell comprising introducing into a plant cell a polynucleotide encoding a plant *MutS* homolog, plants and plant cells comprising said hypermutable cell, classified in class 800, subclass 278, for example.
 - II. Claims 1, 2, 4, 14, 18, 19, 26, 28, 34, 41, 43, 47, 49, 53, 77, 83 and 84, drawn to a method of making a hypermutable cell comprising introducing into a plant cell a polynucleotide encoding a plant *MutL* homolog, plants and plant cells comprising said hypermutable cell, classified in class 800, subclass 278, for example.
 - III. Claims 1, 2, 15-21, 31-36, 46, 47, 56, 77-79 and 83-85, drawn to a method of making a hypermutable cell comprising introducing into a plant cell a polynucleotide encoding a mammalian *PMS2* gene, plants and plant cells comprising said hypermutable cell, classified in class 800, subclass 288, for example.
 - IV. Claims 1, 2, 6, 18, 19, 22, 34, 37, 47, 77, 80, 83 and 84, drawn to a method of making a hypermutable cell comprising introducing into a plant cell a polynucleotide encoding a mammalian *MLH1* gene, plants and plant

cells comprising said hypermutable cell, classified in class 800, subclass 288, for example.

- V. Claims 1, 2, 7, 23, 38, 47, 77, 81, 83 and 84, drawn to a method of making a hypermutable cell comprising introducing into a plant cell a polynucleotide encoding a mammalian *PMS1* gene, plants and plant cells comprising said hypermutable cell, classified in class 800, subclass 288, for example.
- VI. Claims 1, 2, 8, 24, 39, 47, 77, 82, 83 and 84, drawn to a method of making a hypermutable cell comprising introducing into a plant cell a polynucleotide encoding a mammalian *MSH2* gene, plants and plant cells comprising said hypermutable cell, classified in class 800, subclass 288, for example.
- VII. Claims 1, 2, 9, 18, 19, 34, 47, 77, 82, 83 and 84, drawn to a method of making a hypermutable cell comprising introducing into a plant cell a polynucleotide encoding a eukaryotic *mutS* gene, plants and plant cells comprising said hypermutable cell, classified in class 800, subclass 278, for example.
- VIII. Claims 1, 2, 10, 18, 19, 34, 47, 77, 83 and 84, drawn to a method of making a hypermutable cell comprising introducing into a plant cell a polynucleotide encoding a eukaryotic *mutL* gene, plants and plant cells comprising said hypermutable cell, classified in class 800, subclass 278, for example.

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- IX. Claims 1, 2, 11, 18, 19, 34, 47, 77, 83 and 84, drawn to a method of making a hypermutable cell comprising introducing into a plant cell a polynucleotide encoding a prokaryotic *mutS* gene, plants and plant cells comprising said hypermutable cell, classified in class 800, subclass 278, for example.
- X. Claims 1, 2, 12, 18, 19, 34, 47, 77, 83 and 84, drawn to a method of making a hypermutable cell comprising introducing into a plant cell a polynucleotide encoding a prokaryotic *mutL* gene, plants and plant cells comprising said hypermutable cell, classified in class 800, subclass 278, for example.
- XI. Claims 1, 2, 18, 19, 29, 34, 44, 47, 54, 77, 83 and 84, drawn to a method of making a hypermutable cell comprising introducing into a plant cell a polynucleotide encoding a prokaryotic *MutS* homolog, plants and plant cells comprising said hypermutable cell, classified in class 800, subclass 288, for example.
- XII. Claims 1, 2, 18, 19, 30, 34, 45, 47, 54, 77, 83 and 84, drawn to a method of making a hypermutable cell comprising introducing into a plant cell a polynucleotide encoding a prokaryotic *MutL* homolog, plants and plant cells comprising said hypermutable cell, classified in class 800, subclass 288, for example.

- XIII. Claims 47, 50, 52, 77, 83 and 84, drawn to a hypermutable transgenic plant comprising a mammalian *MutS* homolog, classified in class 800, subclass 298, for example.
- XIV. Claims 47, 51, 53, 77, 83 and 84, drawn to a hypermutable transgenic plant comprising a mammalian *MutL* homolog, classified in class 800, subclass 298, for example.
- XV. Claims 57-76, drawn to a method of generating a mutation in a gene of interest in a plant cell, classified in class 435, subclass 468, for example.
- XVI. Claims 86, 87, 90, 91, 93 and 105, drawn to a method of generating a hypermutable plant comprising inhibiting endogenous mismatch repair activity of a plant, wherein the endogenous plant *MutS* homolog is inhibited by introducing a plant *MutS* gene, classified in class 800, subclass 278, for example.
- XVII. Claims 86, 88, 89, 92, 94 and 105, drawn to a method of generating a hypermutable plant comprising inhibiting endogenous mismatch repair activity of a plant, wherein the endogenous plant *MutL* homolog is inhibited by introducing a plant *MutL* gene, classified in class 800, subclass 278, for example.
- XVIII. Claims 86, 95 and 97-99, drawn to a method of generating a hypermutable plant comprising inhibiting endogenous mismatch repair activity of a plant, wherein the endogenous plant *MutS* homolog is

inhibited by introducing a MutS gene from a lower organism, classified in class 800, subclass 288, for example.

- XIX. Claims 86, 96 and 100-102, drawn to a method of generating a hypermutable plant comprising inhibiting endogenous mismatch repair activity of a plant, wherein the endogenous plant MutL homolog is inhibited by introducing a MutL gene from a lower organism, classified in class 800, subclass 288, for example.
- XX. Claims 86 and 103, drawn to a method of generating a hypermutable plant comprising inhibiting endogenous mismatch repair activity of a plant, wherein the endogenous plant MutL homolog is inhibited by introducing a MutL gene from a rodent, classified in class 800, subclass 288, for example.
- XXI. Claims 86 and 104, drawn to a method of generating a hypermutable plant comprising inhibiting endogenous mismatch repair activity of a plant, wherein the endogenous plant MutS homolog is inhibited by introducing a MutS gene from a rodent, classified in class 800, subclass 288, for example.
- XXII. Claims 106-114, drawn to a plant transformation vector comprising a human PMS134 allele, classified in class 435, subclass 320.1, for example.

- XXIII. Claims 106-112 and 115, drawn to a plant transformation vector comprising an *Arabidopsis* PMS134 allele, classified in class 435, subclass 320.1.
- XXIV. Claims 116 and 117, drawn to an isolated polynucleotide encoding an *Arabidopsis* PMS2, classified in class 536, subclass 23.6, for example.
- XXV. Claims 118 and 119, drawn to an isolated polynucleotide encoding an *Arabidopsis* PMS 134, classified in class 536, subclass 23.6, for example.
- XXVI. Claim 120, drawn to an isolated *Arabidopsis* PMS2 protein, classified in class 530, subclass 370, for example.
- XXVII. Claim 121, drawn to an isolated *Arabidopsis* PMS134 protein, classified in class 530, subclass 370, for example.
- XXVIII. Claims 122-125, drawn to a method of detecting the presence of a mismatch repair defect in a plant or plant cell, classified in class 435, subclass 6, for example.

Claims 1, 2, 18, 34, 47, 77, 83 and 84 are generic to groups I-XIV. Claim 52 is generic to groups I and XIII. Claim 53 is generic to groups II and XIV. Claim 86 is generic to groups XVI-XXI. Claim 106 is generic to claims XXII and XXIII. Generic claims will be examined to the extent that they read upon the elected invention.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions I-XIV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In

the instant case the different inventions are unrelated because the method of any one of Groups I-XII cannot be used to produce the plant of any other group, and the plant of any one of Groups I-XIV is structurally, compositionally and functionally distinct from that of any other group.

3. Inventions I-XIV and XV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the method of Group XV can be practiced using a materially different product, such as a naturally occurring mutant, non-transgenic plant wherein said mutant, non-transgenic plant comprises a dominant negative allele of a mismatch repair gene.

4. Inventions I-XIV and XVI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because the transgenic plant of any one of Groups I-XIV cannot be made using the method of Group XVI, and the product of the method of Group XVI has a different mode of operation than that of the transgenic plant of any one of Groups I-XIV.

5. Inventions I-XIV and XVII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP §

808.01). In the instant case the different inventions are unrelated because the transgenic plant of any one of Groups I-XIV cannot be made using the method of Group XVII, and the product of the method of Group XVII has a different mode of operation than that of the transgenic plant of any one of Groups I-XIV.

6. Inventions I-XIV and XVIII and XIX are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because the transgenic plant of any one of Groups I-XIV cannot be made using either the method of Group XVIII or XIX.

7. Inventions I-XII and XX and XXI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because the transgenic plant of any one of Groups I-XII cannot be made using the method of either XX or XXI.

8. Inventions XIII and XXI are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the method

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of Group XIII does not require the rodent gene of Group XXI. The subcombination has separate utility such as a method of expressing a rodent protein in a plant.

9. Inventions XIV and XX are related as combination and subcombination.

Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the method of Group XIV does not require the rodent gene of Group XX. The subcombination has separate utility such as a method of expressing a rodent protein in a plant.

10. Inventions I-XIV, XV-XXI and XXII and XXIII are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the plant transformation vector of either Group XXII or XXIII can be used in a materially different process than that of producing the plant of any one of Groups I-XIV or XV-XXI, such as in a Southern hybridization method or a library screening method.

11. Inventions I-XIV and XXIV and XXV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because the

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isolated polynucleotide of either Group XXIV or XXV cannot be used to make the plant of any one of Groups I-XIV.

12. Inventions I-XXV and XXVIII and XXVI and XXVII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because the isolated protein of either Group XXVI or XXVII cannot be used in any of the methods of any one of Groups I-XII, XV-XXI and XXVIII, nor can they be used to produce the products of any one of Groups XIII, XIV, XXII and XXIII.

13. Inventions I-XIV and XXVIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because the method of Group XXVIII cannot be used to make the plant of any of Groups I-XIV.

14. Inventions XV, XVI, XVII, XVIII, XIX, XX, XXI and XXVIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because each of the methods encompassed by Groups XV, XVI, XVII, XVIII, XIX, XX, XXI and XXVIII have different starting materials, different method steps and different effects and functions.

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15. Inventions XXII and XXIII and XXVIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because the plant transformation vector of Group XXII or XXIII cannot be used in the method of Group XXVII.

16. Inventions XXII, XXIII and XXIV, XXVI and XXVII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because the plant transformation vector of either Group XXII or XXIII is structurally, compositionally and functionally distinct from the isolated polynucleotide of Group XXIV and the protein of either Group XXVI or XXVII.

17. Inventions XXII and XXV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are unrelated because the plant transformation vector of Group XXII comprising a human allele is structurally, functionally and compositionally distinct from the isolated polynucleotide encoding an *Arabidopsis* sequence of Group XXV.

18. Inventions XXIII and XXV are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as

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claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because claim 115 of Group XXIII only requires an *Arabidopsis* PMS134 allele, while the isolated polynucleotide of Group XXV encodes a specific polypeptide sequence or has a specific nucleotide sequence. The subcombination has separate utility such as a DNA library probe.

19. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, recognized divergent subject matter, and because the search required for one of the groups is not required for another, restriction for examination purposes as indicated is proper.

20. Applicant is advised that the reply to this requirement to be complete within one month (not less than 30 days) must include an election of the invention to be examined even though the requirement be traversed (37 CFR § 1.143).

21. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR § 1.48(b) and by the fee required under 37 CFR § 1.17(i).

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22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David H. Kruse, Ph.D. whose telephone number is (703) 306-4539. The examiner can normally be reached on Monday to Friday from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Amy Nelson can be reached at (703) 306-3218. The fax telephone number for this Group is (703) 872-9306 Before Final or (703) 872-9307 After Final.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Kim Davis whose telephone number is (703) 305-3015.

A handwritten signature in cursive script, appearing to read "Amy Nelson".

**AMY J. NELSON, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600**

David H. Kruse, Ph.D.
30 September 2002